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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/482,788	01/13/2000	Randy m Berka	5778.200-US	7465

25907 7590 08/19/2004

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EXAMINER	
RAMIREZ, DELIA M	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 08/19/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action	Application No.	Applicant(s)	
	09/482,788	BERKA ET AL.	
	Examiner	Art Unit	
	Delia M. Ramirez	1652	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 12 July 2004 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on _____. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2. ☒ The proposed amendment(s) will not be entered because:

   (a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);

   (b) ☒ they raise the issue of new matter (see Note below);

   (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

   (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____.

3. ☐ Applicant's reply has overcome the following rejection(s): _____.

4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5. ☒ The a)☐ affidavit, b)☐ exhibit, or c)☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: *see attached*.

6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7. ☒ For purposes of Appeal, the proposed amendment(s) a)☒ will not be entered or b)☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

   The status of the claim(s) is (or will be) as follows:

   Claim(s) allowed: *none*.

   Claim(s) objected to: *129,130,144 and 145*.

   Claim(s) rejected: *124-128,131-143 and 146-150*.

   Claim(s) withdrawn from consideration: *none*.

8. ☐ The drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.

9. ☐ Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). _____.

10. ☐ Other: _____

ADVISORY ACTION

1. Claims 124-150 are pending.

2. The period for reply continues to run from the date of the final rejection. Any extension of time must be obtained by filing a petition under 37 CRF 1.136(a) accompanied by the appropriate fee. The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. A reply within the meaning of 37 CFR 1.113 must be timely filed to avoid abandonment of this application.

3. The request for entering amendments to claims 124, 137, 139, 150, cancellation of claims 128, 143, addition of claims 151-168, and arguments filed on 7/12/2004 under 37 CFR 1.116 in reply to the Final Action Paper mailed on 3/19/2004 are acknowledged. Amendments to claims 137 and 150 appear to overcome previous objections. Amendments to claims 124, 139 and cancellation of claims 128 and 143, while overcoming the previous 35 USC 112 first paragraph, written description rejection previously applied to claims 124-127, 131-142 and 146-150, raise new matter issues as discussed below. Furthermore, amendments to the claims are not deemed sufficient to overcome the 35 USC 112 first paragraph, scope of enablement rejection previously applied for the reasons discussed below. Therefore, the proposed amendments to the claims will not be entered.

4. Proposed new claims 152, 154, 161, 163 would be rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement due to the introduction of new matter. New claims 152, 154, 161, 163 are drawn to a method/mutant cells that requires the disruption or deletion of a genus of cyclohexadepsipeptide synthetase genes for which there is no support in the specification as originally filed. The Examiner has been unable to locate adequate support for cyclohexadepsipeptide synthetase genes encoding polypeptides having 75% or 85% sequence identity to the polypeptide of SEQ ID NO: 2. Thus, there is no indication that methods/mutant cells that require the disruption or deletion of

a genus of cyclohexadepsipeptide synthetase genes encoding polypeptides having 75% or 85% sequence identity to the polypeptide of SEQ ID NO: 2 were within the scope of the invention as conceived by Applicants at the time the invention was filed.

5. Proposed amended claims 124-127, 131-142, 146-150 would remain rejected and proposed new claims 155, 157-158, 160-164, 166-167 would be rejected under 35 USC 112, first paragraph, because the specification while being enabling for (1) a method for producing a secreted heterologous polypeptide using a Fusarium venenatum cell, wherein the cell comprises a nucleic acid having a disruption or deletion in a cyclohexadepsipeptide synthetase gene such that said cell produces less cyclohexadepsipeptide synthetase than the corresponding wild type Fusarium venenatum cell, wherein said cyclohexadepsipeptide synthetase gene encodes the polypeptide of SEQ ID NO: 2, and (2) a Fusarium venenatum cell, wherein the cell comprises a nucleic acid having a disruption or deletion in a cyclohexadepsipeptide synthetase gene such that said cell produces less cyclohexadepsipeptide synthetase than the corresponding wild type Fusarium venenatum cell, and wherein said cyclohexadepsipeptide synthetase gene encodes the polypeptide of SEQ ID NO: 2, does not reasonably provide enablement for (a) a method for producing a secreted heterologous protein using a mutant Fusarium venenatum cell wherein said cell comprises a nucleic acid having a disruption or deletion in a Fusarium venenatum cyclohexadepsipeptide synthetase gene, wherein said gene encodes a polypeptide having at least 70%, 75%, 80%, 85% or 90% sequence identity to the polypeptide of SEQ ID NO: 2, or wherein said gene hybridizes to the polynucleotide of SEQ ID NO: 1 under the medium or medium-high stringency conditions recited in the claims, or (b) a mutant Fusarium venenatum cell modified to produce less cyclohexadepsipeptide synthetase than the corresponding wild type Fusarium venenatum cell by disruption or deletion of the cyclohexadepsipeptide synthetase gene, wherein the cyclohexadepsipeptide synthetase gene encodes a polypeptide having at least 70%, 75%, 80%, 85% or 90% sequence identity to the polypeptide of SEQ ID NO: 2, or wherein said gene hybridizes to the polynucleotide of SEQ ID NO:

1 under the medium or medium-high stringency conditions recited in the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. This rejection has been discussed at length in an Office Action mailed on 6/23/2003 and in the Final Action mailed on 3/19/2004.

6. Applicants traverse the instant rejection and indicate that the reasoning provided in the Office Action in regard to the lack of enablement for the full scope of the claims is not sufficient. Applicants further point out that the specification contains disclosure of many techniques known in the art for identifying other cyclohexadepsipeptide synthetase genes and disrupt/delete them. In view of the amendments to the claims, which now are limited to a method/mutant cells which require deletion/disruption of genes encoding cyclohexadepsipeptide synthetases having at least 70% sequence identity to the polypeptide of SEQ ID NO: 2, it is Applicant's contention that this rejection should be withdrawn.

7. Applicant's arguments have been fully considered but are not considered persuasive in regard to the proposed amended claims 124-127, 131-142, 146-150 or proposed new claims 155, 157-158, 160-164, 166-167. The Examiner acknowledges that (1) the instant claims are now directed to a method/mutant Fusarium venenatum cell wherein the genus of genes encoding cyclohexadepsipeptide synthetases have a structural limitation, and (2) the specification and the art provide many techniques to disrupt/delete a gene. However, this is not deemed sufficient to overcome the previous rejection since the specification, as indicated previously, fails to provide any teaching or suggestion as to which are the structural elements in the only cyclohexadepsipeptide synthetase gene (SEQ ID NO: 1) disclosed that can be modified such that one would obtain structural homologs of (a) the gene of SEQ ID NO: 1 which encode cyclohexadepsipeptide synthetases having at least 70%, 75%, 80%, or 90% sequence identity to the polypeptide of SEQ ID NO: 2, or (b) the gene of SEQ ID NO: 1 which hybridize under medium or medium-high conditions to the polynucleotide of SEQ ID NO: 1 and encode cyclohexadepsipeptide

synthetases. The art as previously presented clearly teaches how structural homologs sharing a high degree of sequence similarity may not share the same function. See particularly the teachings of Witkowski et al. (Biochemistry 38:11643-11650, 1999) and Seffernick et al. (J. Bacteriol. 183(8):2405-2410, 2001) where even proteins sharing more than 95% sequence identity do not have the same function. While it is agreed that methods to detect cyclohexadepsipeptide synthetase activity are known, testing the extremely large number of structural homologs of the gene of SEQ ID NO: 1 encompassed by the claims without any teaching or suggestion as to which of those structural homologs (i.e. encoding proteins at least 70% sequence identical to the polypeptide of SEQ ID NO: 2 or hybridizing under the conditions recited) encode proteins with the desired activity would constitute undue experimentation. Therefore, one cannot reasonably conclude that the instant specification enables the full scope of the claims.

8. As correctly pointed out by Applicants in the Remarks section of a communication filed 7/12/2004, claim 137 should have been objected instead of claim 143 due to the recitation of "a third nucleic acid".

9. The rejections/objections to the claims previously applied in the Final Action mailed on 3/19/2004 are, therefore, maintained for the reasons of record in view of the non-entry of the proposed amendments.

10. For purposes of Appeal, the status of the claims is as follows:

Claim(s) allowed: NONE

Claims(s) objected to: 129-130, 144-145

Claim(s) rejected: 124-128, 131-143, 146-150

Claim(s) withdrawn from consideration: NONE

11. Certain papers related to this application may be submitted to Art Unit 1652 by facsimile transmission. The FAX number is (703) 872-9306. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December

28, 1993) (see 37 CFR 1.6(d)). NOTE: If Applicant submits a paper by FAX, the original copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

12. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PMR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Delia M. Ramirez whose telephone number is (571) 272-0938. The examiner can normally be reached on Monday-Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy can be reached on (571) 272-0928. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1234.

Delia M. Ramirez, Ph.D.
Patent Examiner
Art Unit 1652

DR
August 11, 2004

REBECCA E. PRUTY
PRIMARY EXAMINER
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